containing ^{14}C-labeled ethyl malonate. In his experiment using the lichen thallus packed with the solution of diethyl malonate-^{14}C in a glass cylinder, incorporation of radioactivity into the depside was not observed.

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The Synthesis of 1-Alkoxy-, 1-Alkoxy-9-alkyl-, and 9-Alkyladenines

Much interest in the recently discovered preferential alkylation of adenine (IV) on the 3-position[1~4] and of its N-substituted derivatives at the same[*1,1,5,7] or other position[1,4,6~9] stimulated us to investigate the site of alkylation of adenine 1-oxide (I)[10,11] in connection with our current research program. Now we report the synthesis of 9-alkyladenines (VIIa, b, c)[12] from IV, as shown in Chart 1, through the use of the easily removable alkoxy group at the 1-position to orient to the 9-position on alkylation.

Treatment of I with methyl, ethyl iodide, and benzyl bromide in N,N-dimethylacetamide at room temperature furnished the corresponding 1-alkoxyadenine salt (II) as the major product (60~80%): 1-methoxyadenine hydriodide (IIa: X=I), m.p. 222° (decomp.); 1-ethoxyadenine hydriodide (IIb: X=I), m.p. 208° (decomp.); 1-benzyloxyadenine hydrobromide (IIc: X=Br), m.p. 214~219° (decomp.). The salts were readily converted in good yields to the corresponding free bases (III) by the use of Amberlite IR-45 or basification to pH 7.5 (for IIIc): IIIa, m.p. 255~257° (decomp.); IIIb, m.p. 219° (decomp.); IIIc, m.p. 164~166° (decomp.). The 1-alkoxy structure was assignable by the successful catalytic hydrogenolysis of the free bases (IIIa, b, c) to adenine (IV) (84~90%

[*1] In the case of benzylation on N′-benzoyladenine with benzyl bromide, instead of the chloride (Ref. 7), in dimethylacetamide at 90° for 8 hr., we also obtained 3-benzyl-N′-benzoyladenine hydrobromide of m.p. 257~259° (decomp.) in a yield of 57%, which gave (78%) 3-benzyladenine on mild alkaline hydrolysis. A similar observation has been made by B. Shimizu and M. Miyaki (Tetrahedron Letters, No. 25, 2059 (1965).

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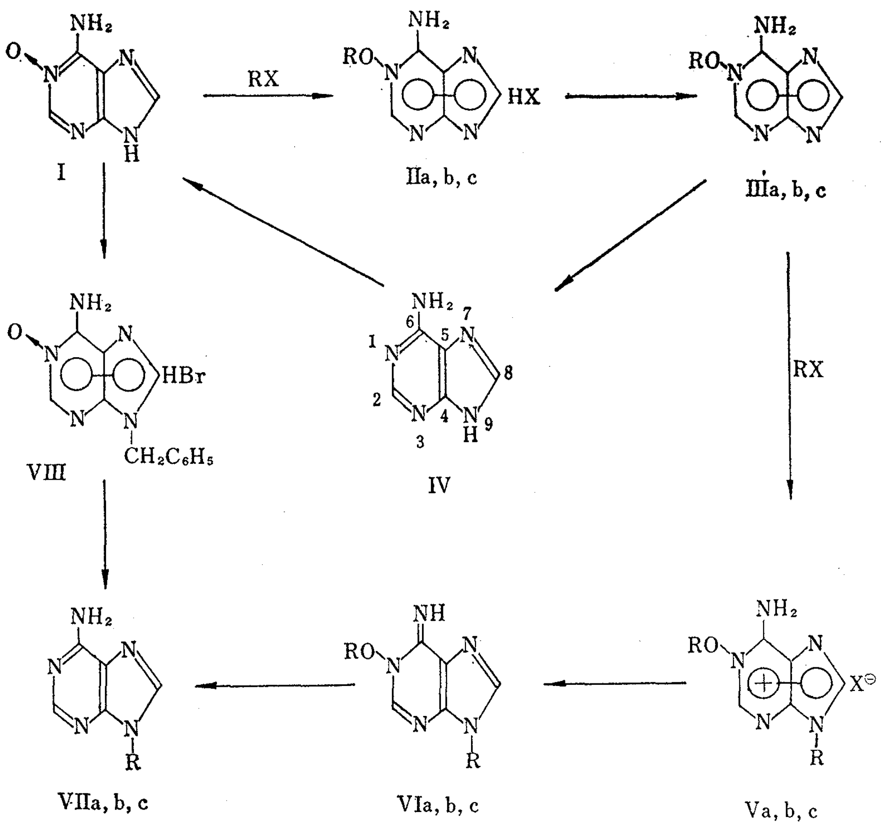

a : $R=CH_3$
b : $R=CH_3CH_2$
c : $R=C_6H_5CH_2$

Chart 1.*2

yield), with uptake of one equivalent mole of hydrogen, in the presence of Raney nickel catalyst. Interestingly, the 1-alkoxyadenines (III) had similar ultraviolet absorption spectra (*e.g.*, IIIa : $\lambda_{\max}^{0.1N\ HCl}$ 258 mμ (ε 11,600), $\lambda_{\min}$ 229 (2,700); $\lambda_{\max}^{0.1N\ NaOH}$ 269 (14,300), $\lambda_{\min}$ 240 (4,100)) to those of 1-alkyladenines.[8,9]

The second alkylation occurred at the 9-position when the 1-alkoxyadenines (IIIa, b, c) were treated again with methyl, ethyl iodide, and benzyl bromide in N,N-dimethylacetamide at room temperature, resulting in the formation (52~70%) of the corresponding 1-alkoxy-9-alkyladenine salts (V) : 1-methoxy-9-methyladenine hydriodide (Va : X=I), m.p. 214~215° (decomp.); 1-ethoxy-9-ethyladenine hydriodide (Vb : X=I), m.p. 186° (decomp.); 1-benzyloxy-9-benzyladenine hydrobromide (Vc : X=Br), m.p. 218° (decomp.). The salts thus obtained had similar ultraviolet absorption spectra (*e.g.*, Va : $\lambda_{\max}^{0.1N\ HCl}$ 260 mμ (ε 12,200), $\lambda_{\min}$ 243 (7,400); $\lambda_{\max}^{0.1N\ NaOH}$ 257 (12,400), $\lambda_{\text{shoulder}}$ 264 (11,200), $\lambda_{\min}$ 243 (8,900)) which resemble to those of 1,9-dialkyladenine salts.[8,9] The location of the second alkyl group was established by hydrogenolysis, using hydrogen and Raney nickel, of the corresponding free bases (VIa, b, c), which led to the formation (67~74%) of 9-alkyladenines (VIIa, b, c) with uptake of one equivalent mole of hydrogen : VIIa, m.p. 303~305°[9]; VIIb, m.p. 193~195°[13]; VIIc, m.p. 233~236°.[1] The directivity of the

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*2 We prefer not to commit ourselves as to tautomeric forms by the designations of structure employed herein, except for those which have been customarily used.

[13] J.A. Montgomery, C. Temple, Jr. : J. Am. Chem. Soc., 79, 5238 (1957).

1-alkoxy substituent in the alkylation described above is parallel to that of the 1-alkyl group reported by Leonard and Fujii.[9]

Further interest in the first alkylation stems from the conversion (57%) of I to 9-benzyladenine 1-oxide hydrobromide (Ⅷ), m.p. 240～243° (decomp.), by the reaction with two mole equivalents of benzyl bromide at an elevated temperature (120°) for 3 hrs. The free base of m.p. 285° (decomp.) obtained from Ⅷ was deoxygenated with hydrogen and Raney nickel to give (95% yield) 9-benzyladenine (Ⅶc), which was obtained also by heating the salt (Ⅷ) in N,N-dimethylacetamide*[3] under reflux for 1 hr.

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*[3] The recently proposed mechanism by E.C. Taylor and E.E. Garcia (J. Am. Chem. Soc., **86**, 4721 (1964)) for the deoxygenation of the 7-N-oxide group of 8-substituted theophyllines in DMF seems not to be applicable to our case.

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Conversion of Enmein to (−)-Kaurane. The Absolute Stereochemistry of Enmein

In the joint paper with several research groups,[1] we have reported the chemical structure of enmein, a diterpene bitter substance from *Isodon trichocarpus* Kudo, is to be formulated as I and this result was ascertained by our X-ray diffractio nstudy.[2] The absolute configuration of enmein has been proposed[1] on the basis of the optical rotatory dispersion data and the conformational analysis and hence enmein was biogenetically considered to be a diterpene homolog of (−)-kaurene. In the present communication, we wish to describe the transformation of enmein into (−)-kaurane (α-dihydro(−)-kaurene)[3,4] through multi-step chemical reactions, which confirms the absolute configuration of enmein with antipodal A/B stereochemistry to steroids.*[1]

Diketolactone methyl ester (Ⅲ), m.p. 212～212.5°, $\nu_{\max}^{\text{KBr}}$ cm^{-1}: 1761, 1714 (*Anal.* Calcd. for $C_{21}H_{28}O_6$: C, 67.00; H, 7.50. Found : C, 67.27; H, 7.47), derived from dihydroenmein (Ⅱ) by a series of reactions mainly described by Kubota, *et al.*,[5] was treated with ethanedithiol at room temperature in the presence of boron trifluoride etherate

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*[1] The recent X-ray study using the anomalous dispersion method has also confirmed this absolute configuration. cf. Y. Iitaka, M. Natsume : Acta Cryst., in press.

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